

IN THE CLAIMS

Please amend the claims as follows:

Claims 1-69 (Canceled).

Claim 70 (Currently Amended): A method for detecting an environmental contaminant or toxin ~~endocrine-disrupting substance, which in combination with an endocrine hormone produces an endocrine disruption, the method~~ comprising:

(A) culturing a cell which is sensitive to [[the]] an endocrine hormone in the presence of an endocrine hormone and a test substance, and detecting a gene expression pattern (1) of said cell;

(B) culturing said cell that is sensitive to the endocrine hormone in the presence of the endocrine hormone, but in the absence of the test substance, and detecting a gene expression pattern (2) of said cell;

(C) culturing said cell that is sensitive to the endocrine hormone in the absence of the endocrine hormone, but in the presence of the test substance, and detecting a gene expression pattern (3) of said cell;

comparing the gene expression pattern (1) with the gene expression patterns (2) and (3) to identify one or more ~~unique gene expressions~~ gene product(s) which is only present in the gene expression pattern (1), ~~but is absent~~ and not present in gene expression patterns (2) and/or (3),

wherein the presence of the at least one ~~unique gene expression~~ gene product only present in gene expression pattern (1) indicates the presence of an environmental contaminant or toxin which is an endocrine disrupting substance ~~that the test compound is an endocrine disrupting substance~~, and

wherein said cell has not been obtained by genetic engineering.

Claim 71 (Previously Presented): The method according to Claim 70, wherein each of the gene expression patterns (1) to (3) is an electrophoretic pattern of transcribed RNAs recovered from the corresponding cultured cell or an electrophoretic pattern of cDNAs corresponding to the transcribed RNAs.

Claim 72 (Previously Presented): The method according to Claim 70, further comprising subtractive hybridization of the transcribed RNA or corresponding cDNA from (A) with complementary cDNA or complementary transcribed RNA from (B) and/or (C) prior to comparing the gene expression pattern (1) with gene expression patterns (2) and/or (3).

Claim 73 (Currently Amended): The method according to Claim 70, further comprising:

(D) culturing said cell that is sensitive to the endocrine hormone in the absence of the endocrine hormone and in the absence of the test substance, and detecting a gene expression pattern (4) of said cell;

checking whether the unique gene ~~expression~~ product(s) expressed in gene expression pattern (1) is present or absent in the gene expression pattern (4),

wherein the absence of the unique gene expression product(s) that are found in gene expression pattern (1) in ~~the~~ gene expression pattern (4) confirms that the test compound is an endocrine disrupting substance.

Claim 74 (Previously Presented): The method according to Claim 73, wherein the gene expression patterns (1) and (4) are electrophoretic patterns of RNAs recovered from (A)

and (D) or from an electrophoretic pattern of cDNAs corresponding to the RNAs recovered from (A) and (D).

Claim 75 (Previously Presented): The method according to Claim 74, wherein subtractive hybridization of nucleic acids of (A) and (D) is conducted prior to the checking step involving the comparison of gene expression patterns (1) and (4).

Claim 76 (Previously Presented): The method according to Claim 71, further comprising:

- (a) recovering RNAs from (A) to (C);
- (b) subjecting the RNAs recovered in step (a) to reverse transcription;
- (c) amplifying reverse transcription products obtained in step (b) by PCR; and
- (d) subjecting PCR products obtained in step (c) to electrophoresis, and
- (e) comparing the electrophoretic patterns of bands obtained from (A) and (B) and/or (C), thereby detecting one or more unique bands specific to the gene expression pattern (1) from (A).

Claim 77 (Previously Presented): The method according to Claim 70, wherein each of the gene expression pattern (1) to (3) is determined by electrophoretically separating proteins or glycoproteins expressed in (A) to (C).

Claim 78 (Previously Presented): The method according to Claim 77, wherein the proteins or glycoproteins expressed in (A) to (C) are electrophoretically separated using SDS-PAGE to determine the respective gene expression patterns.

Claim 79 (Previously Presented): The method according to Claim 77, wherein the proteins or glycoproteins expressed in (A) to (C) are electrophoretically separated using two-dimensional electrophoresis to determine the respective gene expression patterns.

Claim 80 (Previously Presented): The method according to Claim 70, wherein said cell is a germ cell or a nerve cell.

Claim 81 (Previously Presented): The method according to Claim 70, wherein said cell is a normal cell.

Claim 82 (Previously Presented): The method according to Claim 70, wherein said cell is a cancer cell.

Claim 83 (Previously Presented): The method according to Claim 70, wherein said cell is a human cell.

Claim 84 (Previously Presented): The method according to Claim 70, wherein said cell is a non-human cell.

Claim 85 (Previously Presented): The method according to Claim 70, wherein said cell is selected from the group consisting of a murine neuroblastoma cell, a murine uterus carcinoma cell, a murine testicular Leydig cell, a cell derived from testicular Sertoli cells.

Claim 86 (Previously Presented): The method according to Claim 70, wherein said cell is selected from the group consisting of Neuro2a MCF7, TM3, TM4, 15P-1 and S-20Y.

Claim 87 (Previously Presented): The method according to Claim 70, wherein said endocrine hormone is selected from the group consisting of a female hormone, a male hormone, an adrenal cortex hormone, and an amino acid derivative hormone.

Claim 88 (Previously Presented): The method according to Claim 70, wherein said hormone is selected from the group consisting of estrogen, estradiol, progesterone, androgen, testosterone, androsterone, cortisol, aldosterone, corticosterone, cortisone, triiodothyronine (T3), Thyroxine (T4), and parathyroid hormone.

Claim 89 (New): The method of Claim 70, wherein said environmental contaminant or toxin is present in the test sample at a concentration of one part per billion (ppb) to one part per trillion (ppt).

Claim 90 (New): A method for detecting an endocrine disrupting substance that in combination with a non-estrogen endocrine hormone produces an endocrine disruption, comprising:

(A) culturing a cell which is sensitive to a non-estrogen endocrine hormone in the presence of a non-estrogen endocrine hormone and a test substance, and detecting a gene expression pattern (1) of said cell;

(B) culturing said cell that is sensitive to the non-estrogen endocrine hormone in the presence of the non-estrogen endocrine hormone, but in the absence of the test substance, and detecting a gene expression pattern (2) of said cell;

(C) culturing said cell that is sensitive to the non-estrogen endocrine hormone in the absence of the non-estrogen endocrine hormone, but in the presence of the test substance, and detecting a gene expression pattern (3) of said cell;

comparing the gene expression pattern (1) with the gene expression patterns (2) and (3) to identify one or more gene product(s) which is only present in the gene expression pattern (1), and not present in gene expression patterns (2) and/or (3),

wherein the presence of the at least one gene product only present in gene expression pattern (1) indicates the presence of an environmental contaminant or toxin which is an endocrine disrupting substance, and

wherein said cell has not been obtained by genetic engineering.

Claim 91 (New): The method of Claim 90, wherein said environmental contaminant or toxin is present in the test sample at a concentration of one part per billion (ppb) to one part per trillion (ppt).